Exhibit A

OPEN

Journal of Occupational and Environmental Medicine, Publish Ahead of Print

DOI: 10.1097/JOM.0000000000001800

Serous Ovarian Cancer Caused by Exposure to Asbestos in Cosmetic Talc Powders – A Case Series

Serous Ovarian Cancer Caused by Asbestos in Cosmetic Talc

Joan E. Steffen[1], B.A.; Triet Tran[1], B.A., B.S.; Muna Yimam[1], B.S.; Kate M. Clancy[1,2]; Tess B. Bird[1,3], DPhil; Mark Rigler[4], PhD; William Longo[4], PhD; David S. Egilman[1,5], M.D., M.P.H

[1]Never Again Consulting, Attleboro, MA

[2]University of Alaska - Fairbanks, College of Engineering and Mines (student), Fairbanks, AK

[3]Wesleyan University, Mellon Postdoctoral Fellow, Middletown, CT

[4]MAS LLC, Suwanee, GA

[5]Brown University, Warren Alpert Medical School, Department of Family Medicine, Providence, RI

Never Again Consulting

David S. Egilman, 8 N Main St, Ste 404, Attleboro, MA 02703, degilman@egilman.com

Authors' contributions:

Joan E. Steffen contributed to the conception and design of the work; the acquisition, analysis and interpretation of the data; drafting and editing the work; and final approval of the version to be published. Ms. Steffen contributed to medical record review for the patients, dose calculations, and literature review and analysis. She agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Triet Tran contributed to the conception and design of the work; the acquisition, analysis and interpretation of the data; drafting and critically reviewing the work; and final approval of the version to be published. He collaborated with Joan Steffen, Muna Yimam and Dr. Egilman on dose calculations and also contributed to the literature review and analysis. He also worked with Dr. Egilman on the dose-response risk assessment. He agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Muna Yimam contributed to the analysis and interpretation of the data; drafting and editing the work; and final approval of the version to be published. She also contributed with Triet Tran, Joan Steffen, and Dr. Egilman on dose calculations. She agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Kate M. Clancy contributed to the analysis and interpretation of the data; drafting and editing the work; and final approval of the version to be published. She also contributed to the literature review and analysis. She agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Tess B. Bird contributed to the analysis and interpretation of the data; drafting and editing the work; and final approval of the version to be published. She also contributed to the literature review and analysis. She agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Mark Rigler contributed to the conception and design of the work; the acquisition, analysis and interpretation of the data; critically revising and editing the work; and final approval of the version to be published. Dr. Rigler performed the tissue analyses for asbestos and talc. He also contributed to the literature review and analysis. He agrees to be accountable for all aspects of the work in ensuring that

questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

William Longo contributed to the conception and design of the work; the acquisition, analysis and interpretation of the data; critically revising and editing the work; and final approval of the version to be published. Dr. Longo performed analysis of talc powder for asbestos (reported for Case #3). He agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

David S. Egilman contributed to the conception and design of the work; the analysis and interpretation of the data; drafting and critically revising the work; and final approval of the version to be published. Dr. Egilman examined and interviewed the living patients, contributed to medical record review and performed patient dose calculations. He also contributed to the literature review and analysis. He agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Acknowledgements: We thank Sander Greenland for his review of our risk model and dose calculation equations. Any errors are our responsibility

Funding: Plaintiffs' attorneys in litigation against Johnson & Johnson (Ingham et. al. vs. Johnson & Johnson et. al.) paid for tissue analysis for talc and asbestos in patient tissues. They also paid for travel costs and time spent examining and interviewing patients. There was no outside funding for work on this manuscript.

Institution and Ethics approval and informed consent: There was no requirement for ethics review or institutional review board approval because this research was not experimental and was originally conducted pursuant to a lawsuit. Informed consent was obtained from all living patients. For one deceased patient (Case #8), consent was obtained from the surviving spouse. For the remaining two deceased patients (Case #4 and Case #9), authors relied only on public information revealed during court proceedings.

Disclosure (Authors): Triet Tran, Joan Steffen, Kate Clancy, Muna Yimam and Tess Bird work for Dr. David Egilman, who served as an expert witness in litigation at the request of people who were injured as the result of using talcum powders. Mr. Tran, Ms. Steffen, Ms. Clancy, Ms. Yimam and Dr. Bird were not compensated by law firms for work on this paper and the lawyers for the injured plaintiffs did not review this paper and had no input into the content of the paper.

Dr. David Egilman reports payments from lawyers related to the submitted work. Dr. David Egilman served as an expert witness in litigation at the request of people who were injured as the result of using talcum powders; plaintiffs' lawyers paid for the patient exams taken by Dr. Egilman as part of his expert witness work. He has also served as an expert witness at the request of companies who have been sued for exposure to asbestos from their mines or products. He was not compensated for work on this paper and the lawyers for the injured plaintiffs did not review this paper and had no input into the content of the paper.

Dr. Mark Rigler and Dr. William Longo report payments from lawyers related to the submitted work. Both served as an expert witness in litigation at the request of people who were injured as the result of using talcum powders; they originally performed the tissue analysis for talc and asbestos as part of their expert witness work and were paid by plaintiffs' lawyers for their work. They were not compensated for work on this paper and the lawyers for the injured plaintiffs did not review this paper and had no input into the content of the paper.

Disclaimer: Historic testing of talc for asbestos is limited in methodology and scope. Courts and plaintiff lawyers have agreed, without the knowledge or permission of their clients, to keep secret some of the documents reported here; these documents became public during court proceedings over the objections of J&J and Imerys. Many documents remain sealed.

ABSTRACT

Objective:

Asbestos is a known cause of ovarian cancer. We report 10 cases of serous ovarian cancer among users of Johnson & Johnson (J&J) asbestos-containing "cosmetic" talc products.

Methods:

We conducted an asbestos exposure assessment during talc application and analyzed surgical tissues and talc containers for asbestos and talc.

Results:

Talc was found in all cases and tremolite and/or anthophyllite asbestos was found in 8/10 cases. The asbestos fibers found in the "cosmetic" talc containers matched those found in tissues. We estimated inhaled asbestos dose ranged from 0.38 to 5.18 fiber years.

Conclusion:

We provide evidence that the inhaled dose of asbestos/fibrous talc from "cosmetic" talc use causes ovarian cancer. The unique combination of the types of asbestiform minerals detected in cancerous tissue and "cosmetic" talc is a fingerprint for exposure to asbestos-containing talc.

KEYWORDS

Ovarian Cancer; Asbestos; Talc; Baby Powder; Cosmetics; Johnson & Johnson

INTRODUCTION

Known amongst oncologists as a "silent killer," ovarian cancer is the leading cause of death from all gynecologic cancers and the fifth leading cause of cancer-related deaths among women in the United States.[1] The American Cancer Society estimates that about 22,000 American women will be diagnosed and 13,850 will die of the disease in 2019.[2] In 2010, the agency determined that perineal talc powder use is possibly carcinogenic to humans (group 2b).[3]

Epidemiological studies have examined the relationship between perineal talc use and ovarian cancer. In a 1982 case-control study, Cramer et al. first reported an association between genital talc use and ovarian cancer.[4] At least 32 subsequent epidemiologic studies have examined the association between talc powder use and ovarian cancer.[5-36] High-grade serous carcinoma (HGSC) is the most common form of ovarian cancer and the type of ovarian cancer that has been most consistently associated with perineal use of cosmetic talc products.[6-8,10,12,14,15,24,27,29,32,33,36,37] Meta-analyses have consistently shown an increased risk of HGSC of about 1.3 for perineal talc use.[18,38-40]

Asbestos exposure by inhalation occurs during cosmetic talc use. [41,42] IARC concluded in 2009 that asbestos was a group 1 ovarian carcinogen.[43,44] Dr. H. Wyers' first reported a case of ovarian cancer in a woman with asbestosis in 1949. [45] Twenty-seven epidemiologic studies have since examined the relationship between asbestos exposure and ovarian cancer.[46-72] Nine of these 27 studies report a statistically significant elevation in ovarian cancer risk.[46-48,51,61,62,68,69,71] Epidemiologic findings have demonstrated consistency in different populations: studies of asbestos and ovarian cancer have shown a statistically-significant association among women in different countries with exposures to different types of asbestos fibers and in various occupational and environmental settings.[46-48,51,61,62,68,69,71] Epidemiologic research also suggests a dose-response relationship for asbestos and ovarian cancer when comparing low-exposure and high-exposure subgroups.[47,72] Camargo et al. (2011) performed a meta-analysis of 18 cohort studies of occupational asbestos exposure and reported a pooled standardized mortality ratio (SMR) for ovarian cancer of 1.77 (95% CI, 1.37-2.28).[73]

Epidemiologic studies of talc and ovarian cancer have generally accepted representations by talc mining and manufacturing companies that consumer talc has been asbestos-free since 1976.[6-8,10,12,14,15,24,25,27,29,32,36] However, studies show that consumer talc contains asbestos and a review of the world's largest talc producers records indicated that talc mines contained asbestos, that asbestos cannot be removed from talc, and that talc used in cosmetics was not asbestos-free.[41,74-82] Case control and cohort studies of talc use and ovarian cancer have not differentiated inhalation and perineal talc exposures, and have not considered inhalation exposures in their analyses; this has contributed to misclassification of

exposed cases and inaccurate dose-response assessments.[42] In addition, industry marketing studies from the 1970s indicate that up to 85% of women used talc powders thus many "controls" were probably exposed to asbestos containing talcs. [42,83]

We report ten cases of serous ovarian cancer among users of asbestos-containing J&J cosmetic talc products. Unlike most previous studies on talc and ovarian cancer, we focused on inhalation exposures to asbestos during various talc uses and not perineal exposure. [4,6,12,40] We measured inhalation exposures during perineal application of asbestos-containing cosmetic talc. Based on exposure histories, we estimate the dose of inhaled asbestos and the increase in ovarian cancer risk for each case. Our case series also includes tissue analysis for talc and asbestos in both product and cancer tissue. By synthesizing current knowledge of asbestos carcinogenicity and evidence of asbestos in consumer talc products, our case series provides novel insight into the link between cosmetic talc use and ovarian cancer.

Materials and Methods

We report ten cases of serous ovarian cancer in women who primarily or exclusively used a variety of Johnson & Johnson (J&J) cosmetic talc products including Johnson's Baby Powder (JBP), Shower to Shower (STS), and STS Shimmer. [84]These cases were identified among a group of 22 plaintiffs in Ingham et al. vs. Johnson & Johnson et al. All plaintiffs were diagnosed with ovarian cancer after exposure to J&J cosmetic talc products and TEM tissue analysis for talc and asbestos was performed for 10 of these plaintiffs. We only report on the ten plaintiffs for whom TEM tissue analysis was completed.

There was no requirement for ethics review or institutional review board approval because this research was not experimental and patients participated voluntarily in conjunction with a lawsuit. Informed consent for publication was obtained from all living patients. One patient (Case #8) passed away after her exposure history was collected but before consent for publication was obtained. In this case, consent was obtained from the surviving spouse. For the remaining 2 deceased patients (Case #4 and Case #9), authors relied only on public information revealed during court proceedings. For the exposure assessment, the researcher wore a respirator and was decontaminated post-assessment. The researcher was not exposed to any risk, required to reveal personal information or subjected to specimen collection. The assessment did not meet the requirements to necessitate IRB approval. [85]

Patient Histories

Medical histories, exposure histories (history questionnaire attached as Appendix 1, http://links.lww.com/JOM/A685), and physical examinations were collected for all living patients (8/10 cases). Exposure histories included questions about talc powder use and other sources of asbestos

exposure. We analyzed the frequency and duration of talc uses for each case. For the two deceased patients (Case #4 and Case #9), a rough exposure history was compiled from the testimony of relatives who were familiar with each patient. Available medical records were also reviewed for all cases.

EXPOSURE ASSESSMENT- PERINEAL APPLICATION

The exposure assessment was completed in a 15'x15'x8' room with appropriate negative asbestos airflow technology. The experiment was videotaped using two Sony Model HDR-CX900 cameras with alternating Tyndall and standard lighting. (See Appendix 2, http://links.lww.com/JOM/A686.) Area and background samples were collected using four high-volume area sampling pump stations set up 5' to 6' from the talc user; these pump stations used 25mm air cassettes containing 0.8μm pore size mixed cellulose ester (MCE) filters with 5.0μm backing pads and were calibrated to run at 10 liters/minute. Personal samples were collected using four low-volume pumps affixed to the talc user with the cassettes adjusted to be in the breathing zone of the investigator; the "personal" pumps were calibrated to 2.5 liters/minute. During the experiment, air samples were collected for 5 minutes from all sources.

A researcher wearing personal protective equipment and "personal" air pumps used a metal container of JBP for the experiment. Based on JBP advertisements featuring product images, we estimated that the JBP used in this test had been manufactured sometime in the 1950s and sourced from the Val Chisone mine. [86,87](See Appendix 3, http://links.lww.com/JOM/A688 for images of JBP product tested and for full written report on exposure assessment.) J&J used this mine source from 1946 until 1968 and 1980-1981. [86-88] From 1969 to 2003, J&J used Vermont talc in their powder products and later switched to Chinese. [42,89] Using t-test analysis, the asbestos content (fibers per gram) in all the bottles tested were statistically comparable across these three talc sources. (See Appendix 4, http://links.lww.com/JOM/A689)

The JBP can was weighed before the experiment using a Fisher Scientific balance. The researcher wore a bikini bottom over an inner pair of boxer briefs and sat on a chair in the middle of the room for the experiment. To simulate perineal talc application, the researcher shook the talc powder into his hand twice and then rubber the powder into the upper leg area. This was repeated for the other leg. Then, the researcher stood, pulled the bikini bottom down and away from the body, and applied 2 squeezes of talc powder into the bikini bottom. The researcher released the briefs into place and sat down on the chair for the remainder of the study. The metal container of JBP was weighed again following the study. After the study, 2 field blanks were opened inside the study room.

A total of four background samples, four personal samples, and four area samples were collected along with two field blanks. All twelve air samples were analyzed for asbestos by the NIOSH 7400 PCM

method using "A" counting rules and by the NIOSH 7402 TEM method.[90,91] For TEM analysis, amphibole asbestos fibers or bundles with substantially parallel sides and an aspect ratio of 3:1 or greater, at least longer than 5.0 µm in length and greater than 0.25 µm were counted as per NIOSH 7402 asbestos structure sizing rules.[91] The four personal air samples were also analyzed by the NIOSH 7402 method for fibrous talc particles.[91] The two field blanks were analyzed for asbestos by PCM and TEM in accordance with NIOSH 7400 and NIOSH 7402.[90,91]

DOSE CALCULATIONS

For each case, we calculated asbestos dose in environmental fiber years (for consistency with the EPA risk assessment model) and in total fibers inhaled (to account for changes in respiratory intake in infancy vs. adulthood).[92] We used the asbestos dose in environmental fiber years to calculate the excess risk. (See section on Dose-Response Risk Assessment.)

We calculated total asbestos dose based on the four most common usages of J&J talc powder reported among the ten cases: perineal application (10/10), upper body powdering (9/10), exposure as an adult during diapering (8/10) and exposures as an infant during diapering (7/10). For each of these scenarios, we incorporated the intensity of the exposure (f/cc), duration of each exposure (minutes) and total number of applications (from exposure histories) to calculate the dose. Although we did not adjust for latency, we excluded exposures that occurred after ovarian cancer diagnosis. Fibrous talc exposures from powdering was excluded from our calculations except exposure from baby diapering.[41] Dement et al. (1972) did not differentiate type of fiber detected. [93]

For perineal powdering exposures, we relied on measurements from our exposure assessment. (See above.) Air samples were collected over the course of 5 minutes in this test.

For upper body powdering, we used Gordon et al.'s (2014) measurements for shaker application of cosmetic talc powder to the underarm, shoulder, and upper arm area.[41] Gordon et al. (2014) used Cashmere Bouquet, which used the same Italian mine source as J&J (Val Chisone) from 1940 until 1992. [94,95] Gordon et al. (2014) found that users were exposed to 1.9 f/cc of asbestos fibers over the course of 5 minutes.[41]

For exposures during diapering, Dement et al. (1972) from NIOSH found that an adult is exposed to 2.2 f/cc and that a baby is exposed to 1.8 f/cc over the course of two minutes.[93] When subjects reported that their parents had used talc on them during diaper changes as an infant, we relied on diaper changing norms to estimate infant exposures. US market research and survey data shows that diaper changes typically occur 8-10 times per day for infants (0-6 months) and 4-6 times per day for toddlers (6-24

months).[96-98] Diaper changing frequency in the US also changed over time: the average number of diaper changes per day over the first 2 years of life dropped from eight times per day in the 1960s to 5-6 times per day by the 1980s due to improvements in disposable diapers and reduction in cloth diaper use.[97,99] Since all of the women in our series were born prior to 1975, we assumed that diaper changes occurred eight times per day for two years.

We calculated the dose for each case in fiber years $\left(\frac{f}{cc} \bullet year\right)$ using the same conversions as Anderson et al (2017).[100] For consistency with the EPA dose-response curve used for our risk assessment, we calculated the total duration of exposure based on a continuous, 24-hour exposure period (525,600 min/year) until date of diagnosis.[92]

Formula 1

We also calculated the total number of asbestos fibers inhaled in each case. For adults, we used the National Research Council (NRC)'s estimate of "an annual inhaled air volume of 7,300 m^3" and formula to convert the dose from fiber years to total fibers.[101] We relied on measurements of infant lung volume from Hall (1955) and on median infant respiratory rates calculated by Fleming et al. (2011) to estimate the total inhaled air volume for infants from age 0 to 2.[102,103] Using time-weighted averages for tidal volume and respiratory rate, we calculated that infants breathed 11,025,072,000 ccs in the first 2 years of life, or 5,512,536,000 ccs per year on average.

Formula 2 & 3:

We added together adult and infant exposures to calculate the exposures in total number of asbestos fibers. See Appendix 5, http://links.lww.com/JOM/A690 for the full dose calculations for each case.

Dose-Response Risk Assessment

We developed a method to apply the EPA dose-response curves for inhaled asbestos and mesothelioma risk to ovarian cancer risk. [92] First, we examined the EPA dose-response table for mesothelioma from environmental asbestos exposure (24-hours, 365 days per year). [92] Utilizing the EPA dose-response estimates, we extrapolated a formula for the line of best fit for mesothelioma risk.

We then identified studies that reported mesothelioma and ovarian cancer rates in the same cohort and calculated comparative risk of mesothelioma versus ovarian cancer for each study.[58,62,63,68,71] (See Table 1.)

Using these studies, we calculated the geometric mean comparative risk of contracting mesothelioma versus ovarian cancer from the same asbestos exposures. We applied this comparative risk to the line of best fit for mesothelioma based on the EPA dose-response data to determine a formula for risk of ovarian cancer.

The subjects of the EPA occupational exposure study were entirely men.[92] Since women are more susceptible to cancer from asbestos exposure, we used Lacourt's (2014) findings comparing the mesothelioma odds ratio (OR) in men versus women with the same exposures to adjust the formula for the increase in cancer risk for women.[104] At total doses >0-0.1 fiber years, women were 1.725 times more likely to have mesothelioma than men.[104] At total doses >0.1-1 fiber years, women were 2.855 times more likely to have mesothelioma than men.[104] We applied these ratios to the EPA dose curve calculated to obtain a better estimate of the ovarian cancer dose-response in women.

The resulting dose-response curve for inhaled asbestos and ovarian cancer is shown in Figure 1. We used each case's asbestos dose estimate in fiber years to identify their relative lifetime risk of developing ovarian cancer along the dose-response curve. We then compared each case's risk of contracting ovarian cancer due to inhaled asbestos exposure to the expected incidence of ovarian cancer for those without asbestos exposure: 11.4 per 100,000 from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program.[105]

Tissue Analysis for Asbestos and Talc

Samples from a combination of the left and right ovaries, left and right fallopian tubes, and left and right pelvic lymph nodes were obtained from the hospital for each of the ten patients. Tissues were analyzed to identify and quantify talc and asbestos content in the tissue.

For tissue analysis, a small portion of the tissue in each block was removed with a clean razor blade and placed in a pre-weighed 20-30 mL borosilicate glass vial. The vial was filled with ten mL of filtered extraction solvent (hexane) and placed in a 60°C water bath. The filtered extraction solvent was replaced every twenty minutes for a total of three changes. After the last extraction solvent change, two changes of filtered ethanol (10 mL, each) ten minutes each were performed, then the tissue piece(s) were dried at 110 – 120°C.

Tissue samples were digested with 15-30 mL of filtered sodium hypochlorite (appx. 8.0% bleach). After digestion, the remaining digested material was filtered through a 25 mm, 0.4 micron polycarbonate (PC) filter. The filter containing the tissue residue was dried and subsequently prepared for TEM examination.

A paraffin control sample (wax blank) was obtained by dissolving a known quantity of the paraffin blocks (devoid of tissue) in ten mL of filtered extraction solvent and the dissolved solvent/wax solution was then filtered onto a twenty-five mm, 0.4 micron PC filter. The filter was allowed to dry and then prepared for TEM analysis. A process blank (sample vial) was prepared in the same manner and followed the wax blank and tissue sample vials through all steps.

For TEM analysis, 100 - 300 grid openings were analyzed for all asbestos and talc structures at a magnification of between 4,000 and 20,000X. As per standard TEM analysis protocols, asbestos fiber/bundle identification was done by morphology (substantially parallel sides and length to width ratio of at least 5:1), length (greater than 0.5 μm in length), selected area electron diffraction (SAED), and energy dispersive X-ray spectroscopy (EDS).[106-112] Talc structures (platy and fibrous) were identified morphologically, by selected area diffraction (SAED), and energy dispersive spectroscopy (EDS).

RESULTS

EXPOSURE ASSESSMENT

Total weight used during the application process was 4.05g of talc powder. For the 5 minute sampling time, the average total fiber exposure was 4.52 f/cc (5.86, 4.38, 3.85, and 3.98 f/cc), the average asbestos exposure was 2.57 f/cc (4.51, 1.88, 2.07, and 1.81 f/cc) and the average talc exposure was 1.95 f/cc (1.35, 2.50, 1.78, and 2.16 f/cc) for the talc user personal samples. For area samples, the average total fiber exposure was 0.41 f/cc (0.52, 0.28, 0.42, 0.40 f/cc), the average asbestos exposure was 0.2 f/cc (0.31, 0.20, 0.13, and 0.16 f/cc) and the average fibrous talc exposure was 0.19 f/cc (0.13, 0.08, 0.29, and 0.24 f/cc). The type of asbestos fiber identified in all samples was tremolite asbestos. No fibers were detected in the background samples or field blanks. The complete exposure assessment report, including count sheets and fiber images, is available as Appendix 3, http://links.lww.com/JOM/A688.

DOSE CALCULATIONS AND RISK ASSESSMENT

Results for dose calculations, risk assessment and tissue analysis are summarized in Table 2. See Appendix 5, http://links.lww.com/JOM/A690 for complete past medical history, history of present illness, other ovarian risk factors, exposure history, and dose calculations for each case.

STS was comprised of talcum powder mixed with cornstarch. The STS products contained between 80% to 100% talc sourced from the same mines as JBP.[84] Only 4 cases used these products for brief or unknown periods of time. Case #3 reported infrequent use of unidentified facial make-up powder, and Case #6 reported infrequent use of generic store-brand talcum powder. We could not calculate exposures for the brief use of these unknown products.

All cases had pathologically confirmed serous ovarian cancer. Age at diagnosis ranged from 41 to 78 years, with a mean age at diagnosis of 51.1 years and median age at diagnosis of 50 years. By contrast, the median age of ovarian cancer diagnosis in the United States is 63 with most cases occurring in women aged 55 to 64. Seven of 10 cases tested negative for BRCA mutations; 2 cases were never tested (#2 and #5) and one case (#8) tested positive for BRCA2 variant L771V.

All cases reported perineal talc application; the frequency of perineal powdering with talc ranged from once per day to ten times per day and the duration ranged from 24 years to 47 years. Nine of ten cases reported upper body powdering with talc ranging from 1 to 5 times per day and lasting from 20 to 47 years. Seven of 10 cases reported that their parents used talc powder on them during diaper changes and eight of 10 cases used talc powder during diapering. The total asbestos dose from talc powder use ranged from 2,774,000,000 to 37,742,501,440 asbestos fibers (0.38-5.18 fiber years) and the average dose was 9,308,551,008 asbestos fibers (1.28 fiber years). No other known asbestos exposure was identified for any of the cases. Based on EPA dose dose-response estimates, the risk of developing ovarian cancer due to inhaled asbestos exposure was calculated to be 2.3 to 31.1 times greater in these cases compared to baseline risk for ovarian.[105] On average, the risk of ovarian cancer increased 7.7-fold among these cases.

TISSUE ANALYSIS

Talc and/or asbestos was identified in the tissue from all cases. Platy talc was found in 9/10 cases (90%) with an average concentration of 264,487 structures per gram (s/g) (range: 0 – 2,057,640 s/g). Fibrous talc was found in 8/10 cases (80%) with an average concentration of 5,878 s/g (range: 0 – 21,545 s/g). Tremolite asbestos was found in 6/10 cases (60%) with an average concentration of 6,488 s/g (range: 0 – 22,000 s/g). Anthophyllite asbestos was found in 4/10 cases (40%) with an average concentration of 2,393 s/g (range: 0 – 12,000 s/g). Ferro-anthophyllite asbestos was also identified in 2 cases (20%), winchite and richterite asbestos were identified in 1 case (10%), and crocidolite asbestos was identified in one case (10%). Two tremolite structures with aspect ratios less than 5:1 were observed in one case, but were not counted as asbestos.

In the 'possible fallopian tube B' tissue of case #2, a cluster measuring 20.0 x 16.0 µm was identified composed of 36 counted talc plates, two fibrous talc structures and one tremolite fiber. (See Figure 2.)

DISCUSSION

This case series identified asbestos and/or talc in the tissue of ten women diagnosed with serous ovarian cancer and exposed to J&J cosmetic talc products. Prior to their ovarian cancer diagnosis, these women were exposed to as much as 2,774,000,000 to 37,742,501,440 asbestos fibers (0.38-5.18 fiber years) due to their use of J&J cosmetic talc products. In all reported cases, asbestos exposures due to J&J talc use resulted in a substantial increase in ovarian cancer risk (2.3-31.1) based on our model. Early median age of diagnosis (50 in this case series versus 63 nationally), and the EPA dose response table, indicates that asbestos exposure in infancy may cause ovarian cancer to occur sooner than it would have occurred absent this exposure. [92] .[105]

The asbestos type found in the perineal talc use inhalation exposure assessment (tremolite asbestos) and the predominant asbestos types identified in these tissue samples (tremolite and anthophyllite asbestos) matched the fiber types previously identified in cosmetic talc products and in talc mines.[41,74,75,77-81] (See Table 3.) Researchers have previously identified anthophyllite asbestos in Johnson's Baby Powder (by TEM analysis),[79] amphibole needles and fibers in baby powder sourced from Vermont,[76,77] and tremolite asbestos fibers in commercial talc produced prior to 1975 from J&J's talc source in Val Chisone, Italy.[81,89]

In 2017, a bundle of tremolite asbestos fibers was found in a bottle of JBP purchased by Case #3 in 2014. (See Appendix 6, http://links.lww.com/JOM/A691 for full purchase report.) Tremolite asbestos was also identified in Case #3's right pelvic lymph node. (See Figure 3.) Winchite and richterite asbestos were found in the tissue in 1 case. However, richterite was called sodium tremolite prior to 1978.[113] Winchite is found in talc from the Allamoore, Texas mine and may have contaminated J&J Italian talc processed at the same plant in the 1970s.[114-118] Similarly, Transite pipes present in Royston Plant may have contaminated J&J talc with crocidolite.[119] [120] Furthermore, Colgate acknowledges that there is crocidolite in some talc.[121]

The most common structures identified by tissue analysis (platy talc, fibrous talc, tremolite and anthophyllite asbestos) strongly indicate talc powder as the source of asbestos exposure in these cases. Tremolite asbestos has had minor commercial production in India and Italy and is mainly found as an accessory mineral in talc, vermiculite, and chrysotile.[122-124] Anthophyllite asbestos, which occurs as an accessory mineral in talc and chrysotile, has also had limited commercial use.[123-125] Anthophyllite and tremolite together account for less than 1% of asbestos production and consumption worldwide.[124]

None of the cases reported in this series had any known history of alternative asbestos or vermiculite exposure and no chrysotile or vermiculite was found in any of the tissue samples. Churg and

Warnock (1979) performed a population study of lung asbestos and noted that "… in women a major source [of asbestos fibers] may be cosmetic talc, which is often contaminated with anthophyllite and tremolite."[126] Finkelstein's (2018) analysis of mesothelial tissue found a statistically significant association for tremolite detected with talc in tissue.[130] This association was higher for females, 82% of whom had talc in their tissue compared to 68% of males. [130] The increased use of talcum-based cosmetics by females, and the similar fiber type combination is a fingerprint of cosmetic talc migrating to the peritoneum. The combination of talc with tremolite and/or anthophyllite asbestos, as identified by Finkelstein (2018) and the ten cases reported here, are a fingerprint for exposure to asbestos-containing talc. [127-129] (Appendix 7, http://links.lww.com/JOM/A692: a chart of fibers detected in J&J compared with fibers in tissue). These results indicate that perineal use can result in important inhalation exposure to asbestos, which is accepted route of transmigration to the peritoneum and ovary.[131]

Our exposure assessment found that cosmetic talc users can be exposed to 2.57 f/cc asbestos in the breathing zone during perineal talc application; this finding was generally in agreement with previous studies of asbestos exposures during talc use. [41,93] The bottle of JBP used in this exposure assessment was tested by TEM which detected 15 million fibers per gram. Further analysis found asbestos in 56/90 JBP bottles with a range of 4,400 to 15,100,000 asbestos fibers per gram (appendix 4, http://links.lww.com/JOM/A689). For comparison, Gordon et al. (2014) conducted exam on 50 samples of a single brand of cosmetic talc, sourced from either Montana, North Carolina or Val Chisone. Gordon et al. (2014) found a range of 1,840 to 200 million asbestos fibers per gram.[41] Asbestos is not evenly distributed in talc ores and sampling cannot be completely representative of exposure. [88,132]

Gordon et al. (2014) selected a bottle with 18 million asbestos fibers per gram for the inhalation study. The results Gordon et al.'s (2014) simulation for body powdering 1.9 f/cc, comparable to our assessment of 2.57 f/cc asbestos exposure per application. Application of cosmetic talc varies greatly, including differences in product, application time, grams per use and location of application. In addition, talc is mined and milled prior to sale, potentially modifying fiber size or dispersing asbestos unequally in finished product. [133] Talc was sourced from various mines and processing methods changed over time, adding to the variability of asbestos content in talc-containing cosmetic products. However, our findings of an asbestos fingerprint in the tissue reveal that regardless of the dose, exposure to talc-containing cosmetic products is sufficient to cause ovarian cancer.

We relied on NIOSH measurements by Dement et al. (1972) to calculate exposures during diapering, however these measurements did not account for airborne asbestos exposures that continued after the sampling time.[93] Dement et al. (1972) collected air samples for two minutes during a simulated

diaper change with JBP, but another experiment in the same study indicated that exposures continued for at least three minutes and likely persisted for even longer.[93] Dement et al. (1972) used phase contrast microscopy and did not differentiate between asbestos and fibrous talc. [93] However, in 1968, NIOSH injected asbestos containing "cosmetic" talc into hamsters and detected tremolite asbestos bodies but no fibrous talc in the animal lungs.[134] Anderson et al. (2017) reported much lower levels during body dusting with talc (0 to 0.0039 f/cc). However, the microscopist in the Anderson et al. study originally identified 4 anthophyllite asbestos fibers in the air samples by TEM, but changed the result to transition fibers at the request of the project supervisor due to concern that the results would be used in litigation.[100,135]

Both our study and Gordon et al.'s (2014) exposures assessment used less talc powder than the average user: these experiments used 4.05 and 0.37 grams of talc respectively, but J&J's unpublished studies found that women used 8.16 grams and men used 13.02 grams of talc powder on average during body powdering.[41,136] Anderson et al. (2017) reported that subjects used 11.6 grams of talc on average to powder their bodies after showering.[100] Therefore, our use estimates were 3 to 20 times lower than Anderson et al. (2017) and J&J's.

We also excluded many reported talc uses from our dose calculations due to a lack of exposure data. For instance, three cases (#1, #3, and #5) regularly used talc powder on their sheets and pillows; several other cases also reported seeing and smelling dust in the air while cleaning the room where they regularly applied talc. (See Appendix 5, http://links.lww.com/JOM/A690 for complete exposure histories.) Although our findings indicate that asbestos is present in consumer talc products at a level sufficient to cause disease, our dose estimates may under or over estimate the total exposure to carcinogens in talc in these cases.

Burns et al. (2019) created a dose estimation-model for cosmetic talc, relying on previous assessments to predict asbestos exposure, including Moon et al. (2011), Gordon et al. (2014), Russell et al. (1979), and Anderson et. al. (2017). [41,100,136-138]Burns et al.'s (2019) assessment was based on an assumption of .1% level of asbestos in talc mathematical model that incorrectly reduced the exposure estimate by 1000. [137] For example, Gordon et al. (2014) reported, 4.8 f/cc, however, Burns et al.'s (2019) math model reduces this figure to 0.0048 f/cc. [41,137] In comparison, Addison et al. (1988) reported that dusts containing 0.1% asbestos may release 1.17-2.79 asbestos fibers/cc into the air, consistent with our measurements.[139]

Our tissue analysis results were consistent with previous reports of asbestos and/or talc in ovarian tissue.[136,140-144] (See Table 4.) The number of asbestos structures per gram, however, were approximately one order of magnitude lower in our study than in previous quantitative studies of asbestos in ovarian

tissue.[143] This discrepancy may be due to differences in tissue preparation and analytical procedures. Other quantitative studies relied on wet tissue weight for their analysis whereas we used a dry weight procedure.[143] Additionally, we counted 100-300 grid openings in our study while other studies appear to have counted the entire grid area.[143] We also found that some tissue samples contained "hot spots" with very high concentrations of asbestos and/or talc compared to the surrounding tissue. (See Figure 2.) The occurrence or absence of "hot spots" may also account for variability in reported asbestos concentrations in tissue. The predominant types of asbestos identified in our series (tremolite and anthophyllite asbestos) are the same as those most commonly reported in past studies.[140,143,144]

We did not consider latency in our risk estimate because our calculations followed the EPA risk assessment, which did not consider latency.[92] In addition, Pira et al. found that for asbestos-caused ovarian cancer "…the SMRs increased monotonically with time since first employment, although the number of deaths was small in several categories..."[68] Our omission of latency from this study is to remain consistent with the EPA assessment and reflect the lack of effect demonstrated by Pira et al.'s analysis.

We omitted fibrous talc from our risk assessment due to a lack of dose-response data in the published literature. IARC has previously classified fibrous talc as a Group 1 carcinogen and OSHA regulates fibrous talc per the asbestos standard.[3,43,145-147] Further research on the relationship between talc powder use and ovarian cancer should include studies of fibrous talc toxicity.

Conclusion

Of the ten reported cases of serous ovarian cancer, all were found to have talc and 8 were found to have asbestos in their tissue samples. The main types of asbestos identified in tissue, tremolite and anthophyllite, constitute a fingerprint for talc containing asbestos and indicate that "cosmetic" talc powder as the source of asbestos exposure in these cases. IARC has concluded that asbestos is an ovarian carcinogen.[43] IARC has likewise classified talc containing asbestiform fibers (including both asbestos and fibrous talc) as a carcinogen.[3,43,148] These cases provide more evidence of the causal link between asbestos, talc, and ovarian cancer and indicate that asbestos is present in consumer talc products at a level sufficient to cause disease.

.In 1973, J&J told the FDA that "Johnson & Johnson's policy of full cooperation with FDA and that if the results of any scientific studies show any question of safety of talc, Johnson & Johnson will not hesitate to take it off the market" and their corporate position is that there is no known safe level of exposure to asbestos.[149] J&J's studies have shown that asbestos has been present in its cosmetic talc ores since the 1950s. In 2019, the FDA has found asbestos in JBP sourced from Vermont

and China and Claire's cosmetics .[150,151] At least three retailers of cosmetic talc accept the causal relationship between talc use and ovarian cancer: Angel of Mine, Perfect Purity, and Assured Body and Foot Powders warn that "frequent application of talcum powder in the female genital area may increase the risk of ovarian cancer."[152] In addition, J&J's talc supplier Rio Tinto Minerals has warned its customers since 2006 of this risk in Material Safety Data Sheets (MSDS) for talc: "perineal use of talc-based body powder is possibly carcinogenic to humans."[153,154] J&J removes this warning from its talc MSDS and cosmetic talc products.[155] Because talc powder is a cosmetic product with no medical benefit, these warnings still do not warrant the sale of a products when the benefits cannot outweigh the risks, especially when there is a safer substitute.[156] [157,158]

J&J should comply with its self-proclaimed obligation to take talc-containing cosmetic products off the market "if the results of any scientific studies show any question of safety of talc, Johnson & Johnson will not hesitate to take it off the market." [149]

SUPPORTING INFORMATION

Appendix 1: Exposure history questionnaire

Appendix 2: Perineal exposure assessment video

Appendix 3: Full report of perineal exposure assessment

Appendix 4: Analysis of historical samples of JBP

Appendix 5: Detail on reported cases

Appendix 6: Report on analysis of JBP purchased by case #3

Appendix 7: Fiber Comparison chart

References

Uncategorized References

1. Gajjar K, Ogden G, Mujahid MI, Razvi K. Symptoms and Risk Factors of Ovarian Cancer: A Survey in Primary Care. *ISRN Obstetrics and Gynecology.* 2012;2012:754197.
2. Society AC. Key Statistics for Ovarian Cancer. 2019; https://www.cancer.org/cancer/ovarian-cancer/about/key-statistics.html. Accessed May 14, 2019.
3. International Agency for Research on Cancer (IARC). Carbon black, titanium dioxide, and talc. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans.* 2010;93:1-413.
4. Cramer DW, Welch WR, Scully RE, Wojciechowski CA. Ovarian cancer and talc: a case-control study. *Cancer.* 1982;50(2):372-376.
5. Booth M, Beral V, Smith P. Risk factors for ovarian cancer: a case-control study. *Br J Cancer.* 1989;60(4):592-598.
6. Chang S, Risch HA. Perineal talc exposure and risk of ovarian carcinoma. *Cancer.* 1997;79(12):2396-2401.
7. Cook LS, Kamb ML, Weiss NS. Perineal powder exposure and the risk of ovarian cancer. *Am J Epidemiol.* 1997;145(5):459-465.
8. Cramer DW, Vitonis AF, Terry KL, Welch WR, Titus LJ. The Association Between Talc Use and Ovarian Cancer: A Retrospective Case-Control Study in Two US States. *Epidemiology.* 2016;27(3):334-346.
9. Cramer DW, Xu H. Epidemiologic evidence for uterine growth factors in the pathogenesis of ovarian cancer. *Ann Epidemiol.* 1995;5(4):310-314.
10. Gates MA, Tworoger SS, Terry KL, et al. Talc use, variants of the GSTM1, GSTT1, and NAT2 genes, and risk of epithelial ovarian cancer. *Cancer Epidemiol Biomarkers Prev.* 2008;17(9):2436-2444.
11. Godard B, Foulkes WD, Provencher D, et al. Risk factors for familial and sporadic ovarian cancer among French Canadians: a case-control study. *Am J Obstet Gynecol.* 1998;179(2):403-410.
12. Harlow BL, Cramer DW, Bell DA, Welch WR. Perineal exposure to talc and ovarian cancer risk. *Obstet Gynecol.* 1992;80(1):19-26.
13. Kurta ML, Moysich KB, Weissfeld JL, et al. Use of fertility drugs and risk of ovarian cancer: results from a U.S.-based case-control study. *Cancer Epidemiol Biomarkers Prev.* 2012;21(8):1282-1292.

14. Merritt MA, Green AC, Nagle CM, Webb PM, Australian Cancer S, Australian Ovarian Cancer Study G. Talcum powder, chronic pelvic inflammation and NSAIDs in relation to risk of epithelial ovarian cancer. *Int J Cancer.* 2008;122(1):170-176.
15. Mills PK, Riordan DG, Cress RD, Young HA. Perineal talc exposure and epithelial ovarian cancer risk in the Central Valley of California. *Int J Cancer.* 2004;112(3):458-464.
16. Ness RB, Grisso JA, Cottreau C, et al. Factors related to inflammation of the ovarian epithelium and risk of ovarian cancer. *Epidemiology.* 2000;11(2):111-117.
17. Purdie D, Green A, Bain C, et al. Reproductive and other factors and risk of epithelial ovarian cancer: an Australian case-control study. Survey of Women's Health Study Group. *Int J Cancer.* 1995;62(6):678-684.
18. Terry KL, Karageorgi S, Shvetsov YB, et al. Genital powder use and risk of ovarian cancer: a pooled analysis of 8,525 cases and 9,859 controls. *Cancer Prev Res (Phila).* 2013;6(8):811-821.
19. Vitonis AF, Titus-Ernstoff L, Cramer DW. Assessing ovarian cancer risk when considering elective oophorectomy at the time of hysterectomy. *Obstet Gynecol.* 2011;117(5):1042-1050.
20. Wu AH, Pearce CL, Tseng CC, Pike MC. African Americans and Hispanics Remain at Lower Risk of Ovarian Cancer Than Non-Hispanic Whites after Considering Nongenetic Risk Factors and Oophorectomy Rates. *Cancer Epidemiol Biomarkers Prev.* 2015;24(7):1094-1100.
21. Pike MC. Hormonal factors and the risk of invasive ovarian cancer: a population-based casecontrol study. *Fertility and sterility.* 2004;82(1):186-195.
22. Chen Y, Wu PC, Lang JH, Ge WJ, Hartge P, Brinton LA. Risk factors for epithelial ovarian cancer in Beijing, China. *Int J Epidemiol.* 1992;21(1):23-29.
23. The Cosmetics Fragrance and Toiletry Association (CTFA). The Cosmetics, Fragrance and Toiletry Association (CTFA) Specifications - Talc & Cosmetic Talc. In:1976.
24. Gertig DM, Hunter DJ, Cramer DW, et al. Prospective study of talc use and ovarian cancer. *J Natl Cancer Inst.* 2000;92(3):249-252.
25. Harlow BL, Weiss NS. A case-control study of borderline ovarian tumors: the influence of perineal exposure to talc. *Am J Epidemiol.* 1989;130(2):390-394.
26. Hartge P, Hoover R, Lesher LP, McGowan L. Talc and ovarian cancer. *JAMA.* 1983;250(14):1844.
27. Houghton SC, Reeves KW, Hankinson SE, et al. Perineal powder use and risk of ovarian cancer. *J Natl Cancer Inst.* 2014;106(9).
28. Moorman PG. Ovarian Cancer Risk Factors in African-American and White Women. *American Journal of Epidemiology.* 2009;170(5).

29. Rosenblatt KA, Weiss NS, Cushing-Haugen KL, Wicklund KG, Rossing MA. Genital powder exposure and the risk of epithelial ovarian cancer. *Cancer Causes Control.* 2011;22(5):737-742.

30. Tzonou A, Polychronopoulou A, Hsieh CC, Rebelakos A, Karakatsani A, Trichopoulos D. Hair dyes, analgesics, tranquilizers and perineal talc application as risk factors for ovarian cancer. *Int J Cancer.* 1993;55(3):408-410.

31. Whittemore AS, Wu ML, Paffenbarger RS, Jr., et al. Personal and environmental characteristics related to epithelial ovarian cancer. II. Exposures to talcum powder, tobacco, alcohol, and coffee. *Am J Epidemiol.* 1988;128(6):1228-1240.

32. Gates MA. Risk Factors for Epithelial Ovarian Cancer by Histologic Subtype. *American Journal of Epidemiology.* 2010;171(1).

33. Wong C, Hempling RE, Piver MS, Natarajan N, Mettlin CJ. Perineal talc exposure and subsequent epithelial ovarian cancer: a case-control study. *Obstet Gynecol.* 1999;93(3):372-376.

34. Rosenblatt KA, Szklo M, Rosenshein NB. Mineral fiber exposure and the development of ovarian cancer. *Gynecol Oncol.* 1992;45(1):20-25.

35. Gonzalez NL. Douching, Talc Use, and Risk of Ovarian Cancer. *Epidemiology.* 2016;27(6).

36. Schildkraut J, Abbott S, Alberg A, et al. Association between Body Powder Use and Ovarian Cancer: The African American Cancer Epidemiology Studies (AACES). *Cancer Epidemiology, Biomarkers & Prevention.* 2016;25(10):1411-1417.

37. Kim J, Park E, Kim O, et al. Cell Origins of High-Grade Serous Ovarian Cancer. *Cancers.* 2018;10:433.

38. Huncharek M, Geschwind JF, Kupelnick B. Perineal application of cosmetic talc and risk of invasive epithelial ovarian cancer: a meta-analysis of 11,933 subjects from sixteen observational studies. *Anticancer Res.* 2003;23(2C):1955-1960.

39. Muscat JE, Huncharek MS. Perineal talc use and ovarian cancer: a critical review. *Eur J Cancer Prev.* 2008;17(2):139-146.

40. Penninkilampi R, Eslick GD. Perineal Talc Use and Ovarian Cancer: A Systematic Review and Meta-Analysis. *Epidemiology.* 2018;29(1):41-49.

41. Gordon RE, Fitzgerald S, Millette J. Asbestos in commercial cosmetic talcum powder as a cause of mesothelioma in women. *Int J Occup Environ Health.* 2014;20(4):318-332.

42. Tran T, Steffen J, Clancy K, Bird T, Egilman D. Talc, Asbestos, and Epidemiology: Corporate Influence and Scientific Incognizance. *Epidemiology.* 2019. In press.

43. IARC. Arsenic, Metals, Fibres, and Dusts - A Review of Human Carcinogens. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans.* 2012;100C.

44. Straif K, Benbrahim-Tallaa L, Baan R, et al. Special Report: Policy. A review of human carcinogens—Part C: metals, arsenic, dusts, and fibres. *The Lancet.* 2009;10:453-454.
45. Wyers H. Asbestosis. *Postgrad Med J.* 1949;25(290):631-638, illust.
46. Acheson ED, Gardner MJ, Pippard EC, Grime LP. Mortality of two groups of women who manufactured gas masks from chrysotile and crocidolite asbestos: a 40-year follow-up. *Br J Ind Med.* 1982;39(4):344-348.
47. Berry G. Mortality from all cancers of asbestos factory workers in east London 1933–80. *Occupational Environment Medicine.* 2000;57.
48. Bulbulyan MA, Ilychova SA, Zahm SH, Astashevsky SV, Zaridze DG. Cancer mortality among women in the Russian printing industry. *Am J Ind Med.* 1999;36(1):166-171.
49. Ferrante D, Bertolotti M, Todesco A, Mirabelli D, Terracini B, Magnani C. Cancer mortality and incidence of mesothelioma in a cohort of wives of asbestos workers in Casale Monferrato, Italy. *Environ Health Perspect.* 2007;115(10):1401-1405.
50. Gardner MJ, Winter PD, Pannett B, Powell CA. Follow up study of workers manufacturing chrysotile asbestos cement products. *Br J Ind Med.* 1986;43(11):726-732.
51. Germani D, Belli S, Bruno C, et al. Cohort mortality study of women compensated for asbestosis in Italy. *Am J Ind Med.* 1999;36(1):129-134.
52. Clin B, Morlais F, Dubois B, et al. Occupational asbestos exposure and digestive cancers - a cohort study. *Aliment Pharmacol Ther.* 2009;30(4):364-374.
53. Newhouse ML, Sullivan KR. A mortality study of workers manufacturing friction materials: 1941-86. *Br J Ind Med.* 1989;46(3):176-179.
54. Rosler JA, Woitowitz HJ, Lange HJ, Woitowitz RH, Ulm K, Rodelsperger K. Mortality rates in a female cohort following asbestos exposure in Germany. *J Occup Med.* 1994;36(8):889-893.
55. Tarchi M, Orsi D, Comba P, et al. Cohort mortality study of rock salt workers in Italy. *Am J Ind Med.* 1994;25(2):251-256.
56. Szeszenia-Dabrowska N, Urszula W, Szymczak W, Strzelecka A. Mortality study of workers compensated for asbestosis in Poland, 1970-1997. *Int J Occup Med Environ Health.* 2002;15(3):267-278.
57. Mamo C, Costa G. Mortality Experience in an Historical Cohort of Chrysotile Asbestos Textile Workers. Proceedings from the Global Asbestos Congress; November 19-21, 2004; Waseda University, Tokyo, Japan.
58. Wilczynska U, Szymczak W, Szeszenia-Dabrowska N. Mortality from malignant neoplasms among workers of an asbestos processing plant in Poland: results of prolonged observation. *Int J Occup Med Environ Health.* 2005;18(4):313-326.

59. McDonald JC, Harris JM, Berry G. Sixty years on: the price of assembling military gas masks in 1940. *Occup Environ Med.* 2006;63(12):852-855.

60. Hein MJ, Stayner LT, Lehman E, Dement JM. Follow-up study of chrysotile textile workers: cohort mortality and exposure-response. *Occup Environ Med.* 2007;64(9):616-625.

61. Pira E, Pelucchi C, Piolatto PG, Negri E, Discalzi G, La Vecchia C. First and subsequent asbestos exposures in relation to mesothelioma and lung cancer mortality. *Br J Cancer.* 2007;97(9):1300-1304.

62. Magnani C FD, Barone-Adesi F. Cancer Risk After Cessation of Asbestos Exposure: A Cohort Study of Italian Asbestos Cement Workers. *Occup Environ Med.* 2008;65(3):164-170.

63. Loomis D, Dement J, Wolf S, RIcherdson D. Lung cancer mortality and fibre exposures among North Carolina asbestos textile workers. *Occupational Environment Medicine.* 2009;66:353-542.

64. Reid A, Segal A, Heyworth JS, de Klerk NH, Musk AW. Gynecologic and breast cancers in women after exposure to blue asbestos at Wittenoom. *Cancer Epidemiol Biomarkers Prev.* 2009;18(1):140-147.

65. Harding A-H, Darnton A, Wegerdt J, McElvenny D. Mortality among British asbestos workers undergoing regular medical examinations (1971–2005). *Occup Environ Med.* 2009;66:487-495.

66. Langseth H, Kjaerheim K. Ovarian cancer and occupational exposure among pulp and paper employees in Norway. *Scan J Work Environ Health.* 2004;30(5):356-361.

67. Pira E, Pelucchi C, Buffoni L, et al. Cancer mortality in a cohort of asbestos textile workers. *British Journal of Cancer.* 2005;92:580-586.

68. Pira E RC, Violante FS. Updated Mortality Study of a Cohort of Asbestos Textile Workers. *Cancer Med.* 2016.

69. Reid A, Franklin P, Olsen N, et al. All-cause mortality and cancer incidence among adults exposed to blue asbestos during childhood. *Am J Ind Med.* 2013;56(2):133-145.

70. Vasama-Neuvonen K, Pukkala E, Paakkulainen H, et al. Ovarian cancer and occupational exposures in Finland. *Am J Ind Med.* 1999;36(1):83-89.

71. Wang X, Lin S, Yu I, Qiu H, Lan Y, Yano E. Cause-specific mortality in a Chinese chrysotile textile worker cohort. *Cancer Sci.* 2013;104(2):245-249.

72. Wignall BK, Fox AJ. Mortality of female gas mask assemblers. *British Journal of Industrial Medicine.* 1982;39.

73. Camargo MC, Stayner LT, Straif K, et al. Occupational Exposure to Asbestos and Ovarian Cancer: A Meta-analysis. *Environmental Health Perspectives.* 2011;119(9):1211-1217.

74. Rohl A, Langer A, Selikoff I, et al. Consumer Talcums and Powders: Mineral and Chemical Characterization. *Journal of Toxicology and Environmental Health.* 1976;2:255-284.

75. Paoletti L, Caiazza S, Donelli G, Pocchiari F. Evaluation by electron microscopy techniques of asbestos contamination in industrial, cosmetic, and pharmaceutical talcs. *Regul Toxicol Pharmacol.* 1984;4(3):222-235.

76. Blount A. "Amphibole Content of Cosmetic and Pharmaceutical Talcs" with attached letters and sample key. In:1991:IMERY211157-211165.

77. Blount AM. Amphibole content of cosmetic and pharmaceutical talcs. *Environ Health Perspect.* 1991;94:225-230.

78. Jehan N. Sustainable Management of Mineral Resources with Special Reference to Asbestos and Silica in Northern Pakistan. *National Centre of Excellence in Geology, University of Peshawar.* 2004.

79. Floyd M. Exhibit PLT-00002-0001: Quantitative Analysis Report for Asbestos in Bulk Material TEM. In:2004.

80. Mattenklott M. Asbest in Talkumpudern und Speckstein - heutige Situation. *Gefahrstoffe - Reinhalt der Luft.* 2007;67(7/8):287-291.

81. Ilgren E, Sartorio, Carlo, Hoskins J. Analysis of an Authentic Historical Italian Cosmetic Talc Sample – Further Evidence for the Lack of Cancer Risk *Environment and Pollution.* 2017;6(2).

82. Steffen JE, Tran T, Fassler EA, Egilman DS. Presence of asbestos in consumer talc products: Evaluating a "zero tolerance" policy. APHA; 2017; Atlanta, GA.

83. Wells P. Memo: Johnson and Johnson Baby Powder- Review of Consumer Research. 1973; https://repository.library.brown.edu/studio/item/bdr:967137/.

84. Johnson Ja. 1969 & 1991 Shower to Shower and Specification. 1969; JNJ000280197 & JNJTALC000023772. Available at: https://repository.library.brown.edu/studio/item/bdr:958143/.

85. E-CFR. Electronic Code of Federal Regulations- Title 45- PART 46—Protection of Human Research Subjects. 2018; https://www.ecfr.gov/cgi-bin/retrieveECFR?gp=&SID=83cd09e1c0f5c6937cd9d7513160fc3f&pitd=20180719&n=pt45.1.46&r=PART&ty=HTML#se45.1.46_1104, October 8, 2019.

86. Johnson & Johnson. Happy Mother's Day: Mothers and Children in Our Ads Through the Years. 2012; https://web.archive.org/web/20170511033452/https://www.kilmerhouse.com/2012/05/happy-mothers-day-mothers-and-children-in-our-ads-through-the-years. Accessed June 6, 2017.

87. Johnson & Johnson. Johnson & Johnson and The Adventures of Robin Hood. 2013; https://web.archive.org/web/20161218073707/http://www.kilmerhouse.com/2013/10/johnson-johnson-and-the-adventures-of-robin-hood/. Accessed December 18, 2016.

88. Minnitt RCA, Rice, P.M., Spangenberg, C. Part 1: Understanding the components of the fundamental sampling error: a key to good sampling practice. *The Journal of The Southern African Institute of Mining and Metallurgy.* 2007;107.

89. Johnson & Johnson (J&J). Johnson & Johnson and Johnson & Johnson Consumer Inc.'s Supplemental Answer to Interrogatory No. 3 of Plaintiff's First Set of Interrogatories. In. Jody E Ratcliff v American Honda Motor Co. Inc., et al.: Superior Court for Washington for King County; 2017.

90. National Institute for Occupational Safety and Health (NIOSH). Method 7400, Issue 2: ASBESTOS and OTHER FIBERS by PCM. In:1994.

91. National Institute for Occupational Safety and Health (NIOSH). Method 7402, Issue 2: ASBESTOS by TEM. In:1994.

92. EPA. *Airborne Asbestos Health Assessment Update. In: EPA Office of Health and Environmental Assessment.* 1986.

93. Dement J, Shuler P, Zumwalde R. *Preliminary Report: Fiber Exposure During Use of Baby Powders.* NIOSH Environmental Investigations Branch;1972.

94. Company CP. Defendant Colgate-Palmolive Company's Supplemental Responses And Objections To Plaintiff's Interrogatories 2-5, 7-12, 14-16, 19-22, 24-26, 32-37, and 39-42. *In Re: Personal Injury And Wrongful Death Asbestos Litigation.* 2013.

95. Palmolive C. Formula for Cashmere Bouquet. 1992; https://repository.library.brown.edu/studio/item/bdr:958148/.

96. DeVito M, Schecter A. Exposure Assessment to Dioxins from the Use of Tampons and Diapers. *Environ Health Perspect.* 2002;110(1):23-28.

97. Sauer B, Hildebrandt C, Franklin W, Hunt R. Resource and Environmental Profile Analysis of Children's Diaper Systems. *Environmental Toxicology and Chemistry.* 1994;13(6):1003-1009.

98. Thaman L, Eichenfield L. Diapering: A Global Perspective. *Pediatric Dermatology.* 2014;31(Suppl. 1):15-18.

99. Elzinga K, Mills D. Innovation and Entry in the US Disposable Diaper Industry. *Industrial and Corporate Change.* 1996;5(3):791-812.

100. Anderson EL, Sheehan PJ, Kalmes RM, Griffin JR. Assessment of Health Risk from Historical Use of Cosmetic Talcum Powder. *Risk Analysis.* 2016:n/a-n/a.

101. NRC. *Asbestiform Fibers: Nonoccupational Health Risks.* Committee on Nonoccupational Health Risks of Asbestiform Fibers, Board on Toxicology and Environmental Health Hazards, National Research Council1984.

102. Hall JE. The physiology of respiration in infants and young children. *Proc R Soc Med.* 1955;48(10):761-764.

103. Fleming S, Thompson M, Stevens R, et al. Normal ranges of heart rate and respiratory rate in children from birth to 18 years of age: a systematic review of observational studies. *Lancet.* 2011;377(9770):1011-1018.

104. Lacourt A, Gramond C, Rolland P, et al. Occupational and non-occupational attributable risk of asbestos exposure for malignant pleural mesothelioma. *Thorax.* 2014;69(6):532-539.

105. Surveillance E, and End Results Program. Cancer Stat Facts: Ovarian Cancer. 2016; https://seer.cancer.gov/statfacts/html/ovary.html. Accessed May 14, 2019.

106. *ISO 10312:1995 Ambient air — Determination of asbestos fibres — Direct transfer transmission electron microscopy method.* International Organization for Standardization; 1995.

107. *ISO 13794:1999 Ambient air — Determination of asbestos fibres — Indirect-transfer transmission electron microscopy method.* International Organization for Standardization; 1999.

108. *ISO 22262-2:2014 Air quality — Bulk materials — Part 2: Quantitative determination of asbestos by gravimetric and microscopical methods.* International Organization for Standardization; 2014.

109. EPA. *Asbestos Hazard Emergency Response Act. 40 CFR Part 763, Subpart E – Asbestos Containing Materials in Schools.* Washington, DC: U.S. Environmental Protection Agency; 1987.

110. *ASTM D5756-02(2008), Standard Test Method for Microvacuum Sampling and Indirect Analysis of Dust by Transmission Electron Microscopy for Asbestos Mass Surface Loading (Withdrawn 2017).* West Conshohocken, PA: ASTM International; 2008.

111. *ASTM D5755-09(2014)e1, Standard Test Method for Microvacuum Sampling and Indirect Analysis of Dust by Transmission Electron Microscopy for Asbestos Structure Number Surface Loading.* West Conshohocken, PA: ASTM International; 2014.

112. *ASTM D7712-18, Standard Terminology for Sampling and Analysis of Asbestos.* West Conshohocken, PA: ASTM International; 2018.

113. National Institute for Occupational Safety and Health (NIOSH). Asbestos Fibers and Other Elongate Mineral Particles: State of the Science and Roadmap for Research. In: Department of Health and Human Services - Centers for Disease Control and Prevention, ed. Vol 62. Current Intelligence Bulletin2011.

114. Whittaker Clark & Daniels. Review of Talc Meeting Held at South Kearny. In:1970:WCD002843-002844.

115. Whittaker Clark & Daniels. Inter-Office Correspondence. In:1970:FM-WCD-MOR-KAN 0002325.

116. Ferry DR. Letter to Mr. Robert G. Smith, President, Whittaker Clark & Daniels. In:1970:CAM-163.

117. Rohrbacher RG. *Asbestos in the Allamoore Talc District, Hudspeth and Culberson Counties, Texas.* Geological Circular: Bureau of Economic Geology, University of Texas at Austin;1973.

118. Wylie AG, Huggins CW. Characteristics of a Potassium Winchite-Asbestos from the Allamoore Talc District, Texas. *Canadian Mineralogist.* 1980;18:101-107.

119. Johnson IVJa. Videotaped Deposition of Mathew Sanchez- Tuesday May 8, 2018. 2018; https://repository.library.brown.edu/studio/item/bdr:958150/.

120. Corporation E. Phase I Environmental Site Assessment and Environmental Compliance Assessment of the Johnson & Johnson Consumer Products Facility, Royston, Georgia. 2004; https://repository.library.brown.edu/studio/item/bdr:958149/.

121. al. CHVCPe. Videotaped Deposition of Michael Burke Colgate Palmolive- July 10, 2018. 2019; https://repository.library.brown.edu/studio/item/bdr:958151/.

122. Finley B, Pierce J, Phelka A, et al. Evaluation of tremolite asbestos exposures associated with the use of commercial products. *Critical Reviews in Toxicology.* 2012;42(2):119-146.

123. Alleman J, Mossman B. Asbestos revisited. *Scientific American.* 1997;227:70-75.

124. Virta R. Mineral Commodity Profiles—Asbestos. In: Interior UDot, ed. Reston, Virginia: US Geological Survey (USGS); 2005.

125. Dodson R, Levin J. An Unusual Case of Mixed-Dust Exposure Involving a "Noncommercial" Asbestos. *Environmental Health Perspectives.* 2001;109(2):199-203.

126. Churg A, Warnock, M., . Analysis of the Cores of Ferruginous (Asbestos) Bodies from the General Populations. *Laboratory Investigation.* 1979;40(5):622-626.

127. Henderson DW, Silkin., Langlois, S.L.P, Whitaker, D., . Malignant Mesothelioma. *The Cancer Series.* 1992.

128. Roggli VL. Asbestos Bodies and Nonasbestos Ferruginous Bodies. In: Roggli VL, Sporn TA, Oury TD, eds. *Pathology of Asbestos-Associated Diseases.* New York, NY: Springer New York; 2004:34-70.

129. Glickman L, Domanski L, Maguire T, Dubielzig R, Churg A. Mesothelioma in pet dogs associated with exposure of their owners to asbestos. *Environmental Research.* 1983;32:305-313.

130. Finkelstein M. Malignant Mesothelioma and Its Nonasbestos Causes. *Archives of Pathology & Laboratory Medicine.* 2018;143(6):659-660.

131. Attanoos RL, Gibbs AR. Primary malignant gonadal mesotheliomas and asbestos. *Histopathology.* 2000;37(2):150-159.

132. British Columbia: Ministry of Environment. Technical guidance on Contaiminated Site: Chapter 12 Composite Sample. 2005;12-10.

133. Egilman D. Health Effects of Censored Elongated Mineral Particles: A Critical Review. In: Brisson M, ed. *Detection Limits in Air Quality and Environmental Measurements - STP 1618.* Vol Detection limits in air quality and environmental measurements.2019.

134. Cralley L. Fibrous and Mineral Content of Cosmetic Talcum Products. *American Industrial Hygiene Association Journal.* 1968;29(4):350-354.

135. Egilman D, J. S. Commentary on "Assessment of Health Risk from Historical Use of Cosmetic Talcum Powder". *Accepted for publication New Solutions.* 2018.

136. Russell R. Special Talc Studies - JBP, Respirable Particle Measurements During Adult Usage, Project #0503.01. In:1977:JNJ000886943-000886945.

137. Burns A, Barlow, C., Banducci, A., Unice, K., Sahmel. J.,. Potential Airborne Asbestos Exposure and Risk Associated with the Historical Use of Cosmetic Talcum Powder Products. *Risk Analysis: An International Journal.* 2019;39(10):2272-2294.

138. Moon MC, Park JD, Choi BS, et al. Risk Assessment of Baby Powder Exposure through Inhalation. *Toxicol Res.* 2011;27(3):137-141.

139. Addison J, JMG. D. A comparison of the carcinogenicity of six tremolites using the intraperitoneal injection assay in rats. . In. *Proceedings of the VIIth International Pneumoconiosis Conference.* . Pittsburgh: NIOSH-ILO; 1998.

140. Langer AM. Letter to Dr. Gavin Hildick-Smith, Director of Clinical Research, Johnson & Johnson. In:1971:JNJ000288077-000288078.

141. Graham J, Graham R. Ovarian cancer and asbestos. *Environ Res.* 1967;1(2):115-128.

142. Cramer DW, Welch WR, Berkowitz RS, Godleski JJ. Presence of talc in pelvic lymph nodes of a woman with ovarian cancer and long-term genital exposure to cosmetic talc. *Obstet Gynecol.* 2007;110(2 Pt 2):498-501.

143. Langseth H, Johansen BV, Nesland JM, Kjaerheim K. Asbestos fibers in ovarian tissue from Norwegian pulp and paper workers. *Int J Gynecol Cancer.* 2007;17(1):44-49.

144. Musti M, Massaro T, Cavone D, et al. Exposure to asbestos and risk of occurrence of primary ovarian mesothelioma. Note II: Description of two case studies. *Conference Paper.* 2009.

145. Occupational Safety and Health Administration. OSHA Standard 1915.1000 - Air contaminants. Occup. Safety and Health Standards for Shipyard Employment, Toxic and Hazardous Substances - Air Contaminants. 2017; http://web.archive.org/web/20190401215023/https://www.osha.gov/laws-regs/regulations/standardnumber/1915/1915.1000. Accessed April 1, 2019.

146. Occupational Safety and Health Administration. Part 57-Health and Safety Standards - Metal and Nonmetallic Underground Mines, Miscellaneous Amendments. *Federal Register.* 1974;39(127):24319.

147. Occupational Safety and Health Administration. Part 1910 - Occupational Safety and Health Standards, Subpart G - Occupational Health and Environmental Control. *Federal Register.* 1972;37(202):22139–22163.

148. International Agency for Research on Cancer (IARC). Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs Volumes 1 to 42. In. Vol Supplement No. 71987.

149. Hildick-Smith G. Nashed W. Memo: Johnson & Johnson Meeting with the Commisioner: Substantial Asbestos Can be Allowed Safely in a Baby Powder. 1974; JNJ 000307413. Available at: https://repository.library.brown.edu/studio/item/bdr:841462/.

150. Food and Drug Administration (FDA). AMA Analytical Services, Inc. Summary of Asbestos and Talc Analysis – Claire's 2019; https://www.fda.gov/media/127825/download.

151. Food and Drug Administration (FDA). AMA Analytical Services, Inc. Summary of Asbestos and Talc Analysis – Johnson & Johnson – Baby Powder Lot #22318RB. 2019; https://www.fda.gov/media/131989/download.

152. Images of labels for Angel of Mine and Perfect Purity talc powder products. In:2018.

153. Imerys. Rio Tinto Minerals Talc MSDS. In:2009.

154. Rio Tinto Minerals. Material Data Safety Sheet - Talc, Version 1.0. In:2006:IMERYS042245-042249.

155. Johnson & Johnson. Safety Data Sheet - Johnson's Baby Powder. In:2015:1-7.

156. Johnson & Johnson (J&J). Technological Forecast - Powders. In:1986:JNJ000000523-JNJ000000536.

157. Johnson & Johnson (J&J). Introducing Johnson & Johnson Baby Cornstarch - Advertisement. In:1984:JNJ000060260.

158. Nicholson S. Email to J. James and I. Ahmed, FW: Cornstarch containing JBP (with attachments). In:2016:JNJ000526749-JNJ000526754.

FIGURE LEGENDS

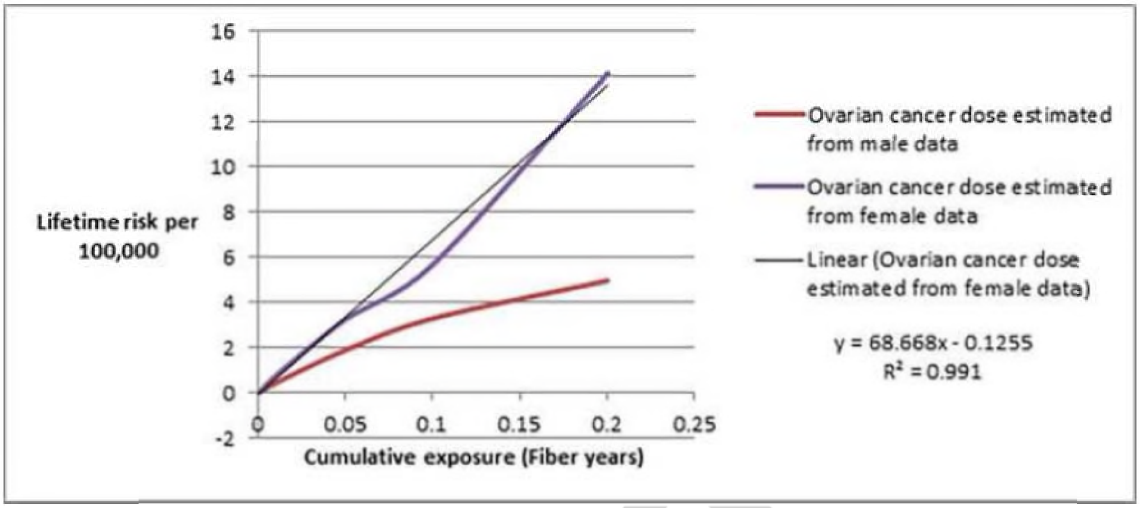

Figure 1: Ovarian cancer dose response (adjusted for difference in female mesothelioma risk)

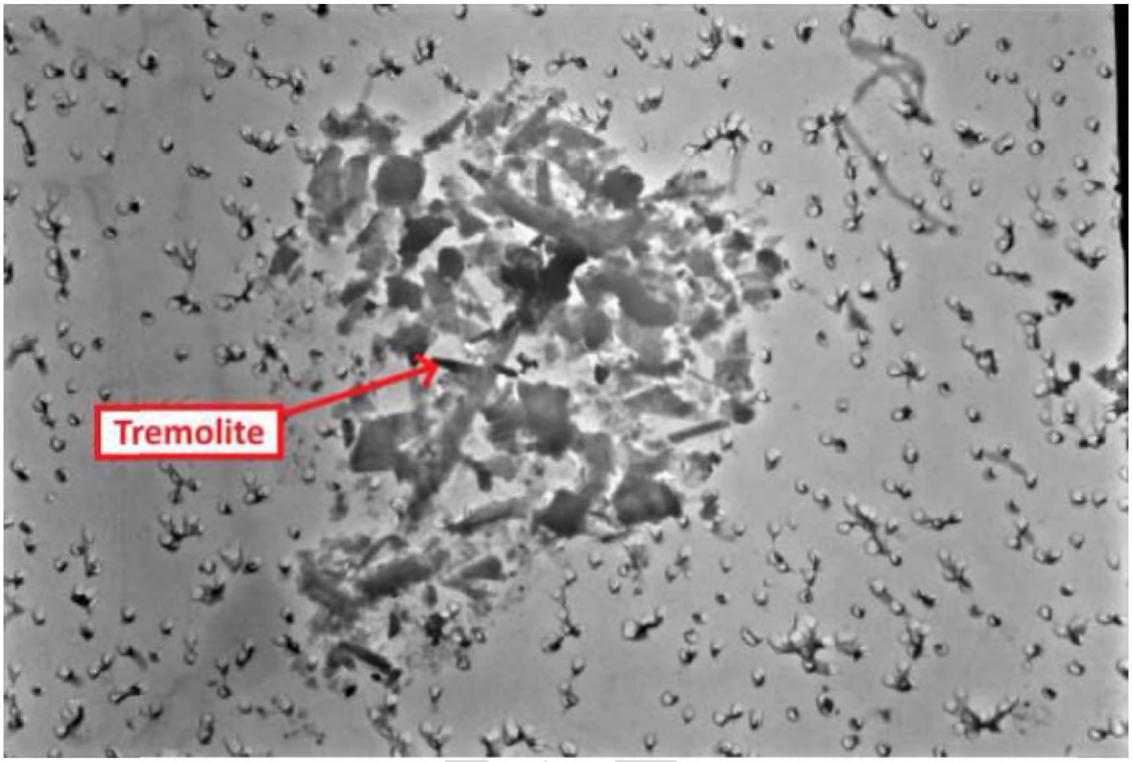

Figure 2: TEM image of cluster measuring 20.0 x 16.0 um composed of 36 counted talc plates, 2 fibrous talc structures and 1 tremolite fiber identified in "possible fallopian tube B" tissue of case #2.

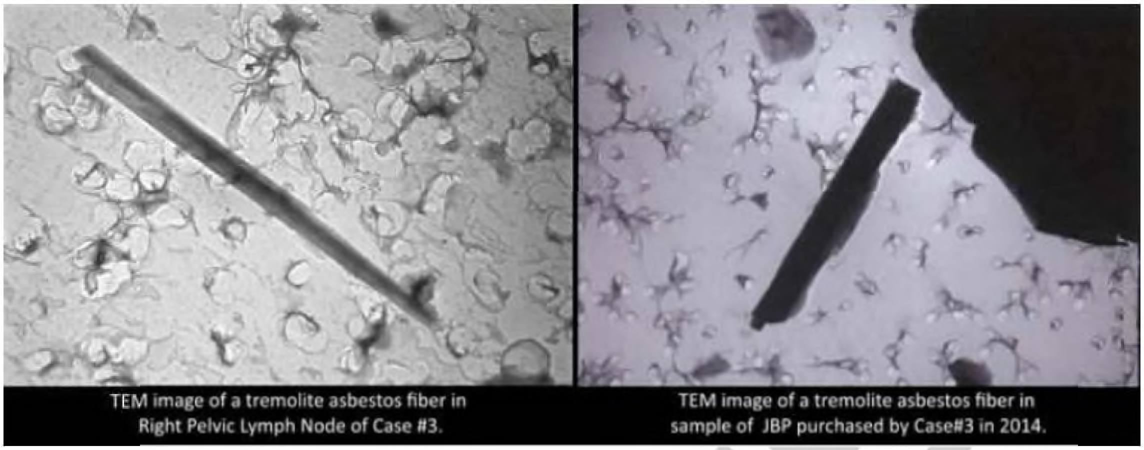

Figure 3: TEM images of a tremolite asbestos fibers in Case #3 right pelvic lymph node tissue (left) and in sample of JBP purchased by Case#3 in 2014 (right).

Table 1: Studies with both mesothelioma and ovarian cancer rates in the same cohort and calculated comparative risk of mesothelioma to ovarian cancer in female-only cohorts.

Study	**Mesothelioma risk (RR)**	**Ovarian cancer risk (RR)**	**Comparative risk M/OC**
Loomis 2009	10.92	1.23	8.88
Magnani 2008	51.49	2.27	22.68
Pira 2016	51.3	3.03	16.93
Wang 2013	166.67	7.69	21.67
Wilczyńska 2005	22.67	1.76	12.88
Geometric mean of comparative risk			15.69

Table 2: Summary of Cases

Case Number	***Diagnosis***	***Age at Diagnosis***	***Talc Exposure History***				***Calculated Asbestos Dose***	***Relative Increase in Ovarian Cancer Risk***	***Pathological Examination***	
			Perineal powdering	*Upper body powdering*	*Infant exposure during diapering*	*Adult exposure during diapering*			*Tissue examined*	*Findings (structures per gram of tissue)*
1	Metastatic high grade papillary serous carcinoma	45	10x/day, 40yrs	5x/day, 40yrs	8x/day, 2yrs	10x/day, 8yrs	37,742,501,440 fibers, (5.18 fiber years)	31.1	Ovary (R)	Platy talc (333 s/g), Fibrous talc (4,000 s/g), Ferro-anthophyllite (3,667 s/g)
									Ovary (L)	Fibrous talc (1,200 s/g), Ferro-anthophyllite (399 s/g)
									Fallopian tube (R)	NSD*
									Fallopian tube (L)	----†
									Pelvic Lymph Node (R)	----†
									Pelvic Lymph Node (L)	NSD*

Case Number	***Diagnosis***	***Age at Diagnosis***	***Talc Exposure History***				***Calculated Asbestos Dose***	***Relative Increase in Ovarian Cancer Risk***	***Pathological Examination***	
			Perineal powdering	*Upper body powdering*	*Infant exposure during diapering*	*Adult exposure during diapering*			*Tissue examined*	*Findings (structures per gram of tissue)*
2	Poorly differentiated high grade serous ovarian carcinoma	53	1x/day, 36yrs	1x/day, 23yrs	8x/day, 2yrs	7.5x/day, 7.5yrs	4,892,501,440 fibers, (0.68 fiber years)	4.1	Ovary A	NSD*
									Ovary B	Platy talc (323 s/g)
									Possible fallopian tube A	NSD*
									Possible fallopian tube B	Platy talc (56,700 s/g), Fibrous talc (4,720 s/g), Tremolite (22,000 s/g)
3	High grade serous carcinoma	49	3x/day, 39yrs	3x/day, 20yrs	8x/day, 2yrs	7x/day, 5yrs	11,535,501,440 fibers, (1.59 fiber years)	9.6	Ovary, fallopian tube (R)	Platy talc (2,001,503 s/g), Fibrous talc (13,343 s/g)
									Adnexa, fallopian tube (L)	Platy talc (12,308 s/g), Fibrous talc (8,202 s/g)

Case Number	***Diagnosis***	***Age at Diagnosis***	***Talc Exposure History***				***Calculated Asbestos Dose***	***Relative Increase in Ovarian Cancer Risk***	***Pathological Examination***	
			Perineal powdering	*Upper body powdering*	*Infant exposure during diapering*	*Adult exposure during diapering*			*Tissue examined*	*Findings (structures per gram of tissue)*
									Pelvic Lymph Node (R)	Tremolite (15,670 s/g), Winchite (15,670 s/g),‡ Richterite (15,670 s/g)‡
									Pelvic Lymph Node (L)	Platy talc (43,829 s/g)
4	Poorly differentiated serous adenocarcinoma	78	1x/day, 43yrs ¶	unknown¶	unknown¶	unknown¶	2,774,000,000 fibers, (0.38 fiber years)	2.3	Ovary (R)	Platy talc (2,860 s/g), Anthophyllite (952 s/g)
									Ovary (L)	Tremolite (604 s/g)
									Fallopian tube (R)	Platy talc (30,000 s/g)
									Fallopian tube (L)	Fibrous talc (868 s/g)
									Pelvic Lymph Node (R)	Platy talc (12,600 s/g)

Case Number	***Diagnosis***	***Age at Diagnosis***	***Talc Exposure History***				***Calculated Asbestos Dose***	***Relative Increase in Ovarian Cancer Risk***	***Pathological Examination***	
			Perineal powdering	*Upper body powdering*	*Infant exposure during diapering*	*Adult exposure during diapering*			*Tissue examined*	*Findings (structures per gram of tissue)*
									Pelvic Lymph Node (L)	Platy talc (17,600 s/g), Tremolite (2,510 s/g)
5	Low grade serous carcinoma	52	1x/day, 47yrs	1x/day, 47yrs	8x/day, 2yrs	10x/day, 10yrs	7,812,501,440 fibers, (1.08 fiber years)	6.5	Ovary (R)	Platy talc (10,900 s/g), Fibrous talc (1,810 s/g)
									Ovary (L)	Platy talc (25,000 s/g), Fibrous talc (5,000 s/g), Tremolite (5,000 s/g)
									Int. Iliac lymph node (R)	Platy talc (77,200 s/g), Fibrous talc (7,720 s/g), Tremolite (3,860 s/g), Anthophyllite (3,860 s/g)

Case Number	***Diagnosis***	***Age at Diagnosis***	***Talc Exposure History***				***Calculated Asbestos Dose***	***Relative Increase in Ovarian Cancer Risk***	***Pathological Examination***	
			Perineal powdering	*Upper body powdering*	*Infant exposure during diapering*	*Adult exposure during diapering*			*Tissue examined*	*Findings (structures per gram of tissue)*
									Comm. Iliac lymph node (R)	Platy talc (50,600 s/g)
6	High grade serous papillary carcinoma	51	1x/day, 40yrs	1x/day, 40yrs	8x/day, 2yrs	10x/day, 10yrs	7,009,501,440 fibers, (0.97 fiber years)	5.8	Adnexa, tumor/ovary (R)	Platy talc (21,300 s/g)
									Adnexa, tumor/ovary (L)	Platy talc (4,720 s/g)
									Adnexa, fallopian tube (R)	Platy talc (12,000 s/g), Tremolite (12,000 s/g), Anthophyllite (12,000 s/g)
									Adnexa, fallopian tube (L)	Platy talc (13,700 s/g)
									Pelvic Lymph Node (L)	Platy talc (11,500 s/g)

Case Number	***Diagnosis***	***Age at Diagnosis***	***Talc Exposure History***				***Calculated Asbestos Dose***	***Relative Increase in Ovarian Cancer Risk***	***Pathological Examination***	
			Perineal powdering	*Upper body powdering*	*Infant exposure during diapering*	*Adult exposure during diapering*			*Tissue examined*	*Findings (structures per gram of tissue)*
7	Serous adenocarcinoma	56	1x/day, 37yrs	1x/day, 37yrs	unknown	7.5x/day, 6yrs	5,183,000,000 fibers, (0.71 fiber years)	4.3	Ovary (R)	Platy talc (8,740 s/g), Fibrous talc (1,090 s/g)
									Ovary (L)	Platy talc (10,500 s/g)
									Fallopian tube (R)	Platy talc (8,500 s/g)
									Fallopian tube (L)	Platy talc (10,900 s/g)
8	High grade ovarian serous carcinoma	44	1x/day, 24yrs	1x/day, 24yrs	unknown	3.5x/day, 4yrs	2,993,000,000 fibers, (0.41 fiber years)	2.5	Ovary (R)	Platy talc (3,340 s/g), Ferro-anthophyllite (1,670 s/g), Crocidolite (1,670 s/g)
									Ovary (L)	Platy talc (799 s/g)

Case Number	***Diagnosis***	***Age at Diagnosis***	***Talc Exposure History***				***Calculated Asbestos Dose***	***Relative Increase in Ovarian Cancer Risk***	***Pathological Examination***	
			Perineal powdering	*Upper body powdering*	*Infant exposure during diapering*	*Adult exposure during diapering*			*Tissue examined*	*Findings (structures per gram of tissue)*
									Fallopian tube (R)	Platy talc (9,690 s/g), Fibrous talc (1,380 s/g), Tremolite (1,385 s/g), Anthophyllite (1,385 s/g)
									Fallopian tube (L)	Platy talc (7,400 s/g), Tremolite (1,850 s/g)
9	Poorly differentiated serous papillary adenocarcinoma§	41	1x/day, 42yrs¶	1x/day, 42yrs¶	8x/day, 2yrs ¶	n/a¶	4,965,501,440 fibers, (0.69 fiber years)	4.1	Ovary (R)	NSD*
									Ovary (L)	NSD*
									Fallopian tube (R)	NSD*
									Fallopian tube (L)	NSD*
									Pelvic Lymph Node (L)	Fibrous talc (8,770 s/g)

Case Number	*Diagnosis*	*Age at Diagnosis*	*Talc Exposure History*				*Calculated Asbestos Dose*	*Relative Increase in Ovarian Cancer Risk*	*Pathological Examination*	
			Perineal powdering	*Upper body powdering*	*Infant exposure during diapering*	*Adult exposure during diapering*			*Tissue examined*	*Findings (structures per gram of tissue)*
10	High-grade ovarian papillary serous carcinoma	42	2x/day, 32yrs	2x/day, 32yrs	8x/day, 2yrs	8x/day, 4yrs	8,177,501,440 fibers, (1.13 fiber years)	6.8	Ovary, fallopian tube (R)	Platy talc (10,800 s/g)#
									Ovary, fallopian tube (L)	Platy talc (5,520 s/g)
									Pelvic Lymph Node (R)	Platy talc (79,300 s/g)
									Pelvic Lymph Node (L)	Platy talc (84,400 s/g)

Table 2 Legend:

* No asbestos or talc structures detected.

† Tissue received, but not analyzed.

‡ Winchite and richterite asbestos were considered tremolite prior to 1978.

¶ Patient deceased; exposure history based on recollections of family and friends.

§ The final pathology report also noted minor components of transitional cell and mucinous carcinoma.

2 tremolite structures were reported with an aspect ratio of less that 5:1 that were not counted.

Table 3: Summary of studies reporting asbestos in consumer talc products

Study	**Test Method**	**Summary of Findings**
Rohl et al (1976)	XRD, PLM, TEM, SEM	0.1-14% tremolite and anthophyllite (mostly fibrous) by weight in 10 of 20 consumer talc products tested
Paoletti et al (1984)	TEM	0.5-1.6% tremolite asbestos in 2 of 6 Italian cosmetic talc powders tested
		Trace to 0.15% chrysotile in 3 of 14, 18.7-21.7% anthophyllite asbestos and tremolite asbestos in 2 of 14, and 0.13% tremolite asbestos & chrysotile in 2 of 10 samples provided by the European Pharmacopeia
Blount (1991)	PLM	10 to 341 structures per mg amphibole fibers, needles, cleavages and 'prismatic pieces' in 9 of 14 samples of pharmaceutical and cosmetic-grade talc powders tested
Jehan (2004)	PLM	Qualitative identification of tremolite asbestos in 13 of 28, chrysotile in 12 of 28, anthophyllite asbestos in 3 of 28, and a mixture of asbestos fibers in 4 of 28 cosmetic talc powder products used in Pakistan
Floyd (2004)	TEM	0.20% anthophyllite asbestos by weight in Johnson's Baby Powder
Mattenklott (2009)	SEM	0.001-0.0073% asbestos by weight in 13 of 57 samples of talc powders sold on the German market from 1996 to 2005
Gordon et al. (2014)	PLM	1,840-1,104,000 fibers per gram asbestos in 50 of 50 historical samples of one brand of cosmetic talc powder tested (40 of 50 contained anthophyllite asbestos only, 4 contained tremolite asbestos only, 4 contained tremolite and anthophyllite asbestos, 2 contained tremolite, anthophyllite, and chrysotile asbestos)
	TEM	0.004-0.9% amphibole asbestos by weight in 9 of 9 samples of the same cosmetic talc product
Ilgren et al (2017)	TEM	3.687 x 10^6 tremolite asbestos fibers/gram in an authentic sample of commercial talc produced prior to 1975 from the talc mine in Val Chisone, Italy

Table 4: Summary of studies finding asbestos and/or talc in ovarian tissue from cosmetic talc use

Study	Tissue Weight Type	Test Method	Summary of Findings
Henderson et al. (1971)	n/a	TEM	Qualitative identification of talc in 10/13 ovarian tumors
			Qualitative identification of talc in 12/21 cervical tumors
Langer (1971)	n/a	Unknown	Qualitative identification of talc and chrysotile asbestos in Henderson et al (1971) samples
Heller, Westhoff et al. (1996)	Wet weight	PLM	26-464 talc particles per gram in 12/12 samples of benign ovarian neoplasms from 12 women with history of adult perineal talc use
			69-420 talc particles per gram in 11/11 samples of benign ovarian neoplasms from 12 women with history of talc diapering during infancy
			6-2,200 talc particles per gram in 6/7 samples of benign ovarian neoplasms from 12 women with no history of adult perineal talc use and an unknown history of other talc uses
		TEM	151,300-7,565,000 talc particles per gram in 5/12 samples of benign ovarian neoplasms from 12 women with history of adult perineal talc use
			151,300-1,600,288 talc particles per gram in 6/11 samples of benign ovarian neoplasms from 12 women with history of talc diapering during infancy
			63,042-1,669,000 talc particles per gram in 3/7 samples of benign ovarian neoplasms from 12 women with no history of adult perineal talc use and an unknown history of other talc uses
Cramer et al. (2007)	n/a	PLM & SEM	Qualitative identification of birefringent particles consistent with talc in pelvic lymph nodes of a 68-year-old woman with stage III ovarian papillary serous carcinoma and a 30-year history of perineal talc use